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Bovine virus diarrhea (BVD) was first recognized in 1946 in the United States and described as an "X" disease of cattle in the same year in Canada. It was reported in Sweden in 1948. In 1953, it was reported by Ramsey and Chivers as a mucosal disease.[12]

When BVD was first recognized, two different conditions were observed and considered to be different diseases. They were Virus Diarrhea and Mucosal Disease. Today it is recognized that all the different conditions of BVD are caused by the same virus of the virus family Togaviridae and genus *Pestivirus*.[3]

Today the occurrence of BVD is worldwide. It may occur in animals of any age, but is generally seen in cattle less than a year of age. In special circumstances it can be devastating to a herd of older cattle, e.g. exposure of a "closed" dairy herd. The morbidity of BVD is high serologically but relatively low clinically. The mortality of the clinical cases, however, is high. In the United Kingdom, 50% of the cattle are seropositive, in Australia 89%, in Germany 87%, and probably a high percentage in the United States.[3]

BVD virus is a highly infectious agent and can be transmitted in several ways. Direct transmission can occur via animal to animal contact, by oral dosing, or by infection, e.g. a contaminated syringe. Indirect transmission can occur through the spread of feces, urine, or nasal secretions by visitors, trucks, or possibly other animals.[2] An inapparent carrier state also exists in which the animal either continuously or periodically sheds the BVD virus.[7,9,13] The incubation period ranges from one to three weeks in the field and is generally around seven days under experimental conditions.[2]

BVD will manifest itself in several ways. Probably the most well known form is as a mucosal disease and/or an enteritis. Abortion, infertility, interdigital hyperkeratosis, weak calves, birth defects, and general lack of condition are also problems encountered with BVD.

The clinical signs vary widely according to the form the disease takes. In the classic case, the animal becomes dull and depressed, usually with anorexia. Rumen stasis is quite common, and the animal may experience mild bloating. As with most viral conditions there is a marked temperature rise which may vary from 104°F to 106°F or higher. The temperature rise may only last one to three days at which time it returns to normal or one to two degrees below normal if not complicated by a secondary bacterial infection. Heart and respiratory rates are usually increased. Two to four days after the onset of the disease, a watery, profuse, foul-smelling diarrhea which may contain mucus and blood begins. The diarrhea is usually very severe and causes rapid dehydration. In peracute cases diarrhea may not be present. Oral lesions are present in 75% of the cases. They begin as small petechial hemorrhages and progress to ulcers or erosions on the lips, tongue, hard and soft palates, gums, nares, and the papillae of the mouth, which they may blunt. In some cases erosions of the coronary and interdigital space may occur. You may see corneal opacity or abortions also.[2,3,12]

The course of the disease varies from two to three days to three weeks with a few animals recovering. Some animals survive, but never completely recover. In these, one may see intermittent diarrhea, chronic bloat,

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rough coat, poor doer, hoof deformities, susceptibility to secondary bacterial infection, and infertility.[13]

The basic lesions of BVD are foci of degenerating epithelial cells. They develop as edema and vasculitis below the epithelial surfaces and progress to erosions. The necrotic foci are found in the mouth, on the gums, in the esophagus (often in a linear arrangement), the forestomachs, the abomasum, and the small and large intestine. Lymphoid necrosis also occurs and may be first evident in the Peyer's patches of the ileum. The nodes may become hemorrhagic and necrotic. Vasculitis may occur in the brain, kidney, liver, or other organs due to the viremia.[2,3,12]

In many cases, other lesions may be found due to secondary infections. These may be seen in acute cases, but are more likely in the chronic ones because of a prolonged immunosuppression. The secondary signs many times can confuse a diagnosis.[20]

The mechanism of action of BVD is very complex and interesting. It causes problems in identifying carriers, treating the disease, and even in preventing the disease. Most of the action is directly or indirectly aimed at the immune system. Its most constant feature is its predilection to replicate in and damage lymphoreticular tissue. This can result in a significant suppression of the animal's specific and nonspecific defense mechanisms against other organisms to which it is simultaneously exposed. This may allow secondary infections. Some may be caused by organisms which are nonpathogenic in other circumstances. As stated before, the clinical signs may not even appear as BVD.[8]

The leukopenia is due in part to BVD's effect on the lymphocyte. BVD virus has a great affinity for cells of the immune system, particularly lymphocytes.[5] Some strains of BVD, like strain C240 (isolated by Gillespie in Oregon in 1960 from a calf spleen), are cytopathic.[10] When they infect an animal and attack its lymphocytes, they rupture and destroy them. In many cases this causes an acute disease and death. Most BVD isolates, however, produce very little or no cytopathic effect (CPE). In fact, when both a cytopathic strain and a non-cytopathic strain are inoculated together, the cytopathic strain many times inhibits the non-cytopathic strain. It is thought that the non-cytopathic virus enters the lymphocytes and may inhibit DNA and RNA synthesis. This inhibition of normal metabolic function may alter the cells' ability to undergo blast transformation in response to oncogenic stimulation. It also interferes with the cells' ability to exercise their normal immunologic action.[15,16] Lymphocyte transformation has been shown to be related to hypersensitivity and cellular immunity which are important in recovery from a viral disease.[16]

A common occurrence in many fatally infected cattle is a complete failure by the cattle to develop detectable BVD virus neutralizing antibodies even though the illness may have been chronic (several months).[15] Their BVD virus infected lymphocytes may become immunologically deficient and permit virus infected cells to persist for the duration of their life span.

Some animals seem to be unaffected even though their lymphocytes are infected by a noncytopathic BVD virus. In a study of a bull infected in utero in a National Animal Disease Center herd, the bull had a persistent infection throughout his life detected by virus isolation from the buffy coat of the blood. He never developed an antibody titer and showed no ill effects ever during his life. The bull did persistently shed virus which was pathogenic to other cattle.[7,20]

Although lymphocyte suppression is a main feature in the pathogenesis of BVD, a study by Ketelsen *et al.* at the University of Minnesota shows a marked depression of the normal response of bovine monocytes to a chemotactic stimulus after these cells are exposed to BVD virus. The alteration of the monocyte function by BVD virus is very rapid, showing that the virus can interact with the monocyte within a few hours after infection. The virus did not cause monocyte lysis, so it is presumed that it somehow alters the cellular metabolism. Killed virus had no effect on the monocytes. Agents which promote macrophage function, like levamisole, have been used to prevent monocyte chemotactic suppression and studies have shown that it can be used to reverse the suppressive effect of BVD in some cases.[10]

The inhibition of neutrophil function is a third way the immune system is altered. In a study done at Iowa State by Doctors Roth, Kaeberle, and Griffith, data indicated that following BVD infection, a defect occurs in PMN function. This might be a result of a

defect in ingestion of particles, degranulation and the release of lysosomal enzymes into the phagosome, or an interference with the myeloperoxidase catalysed reaction. There is also a significant decrease in the number of circulating PMN's. PMN morphology by microscopic examination was not abnormal. It is thought that this action greatly enhances BVD virus survival in the host because PMN's are the most active cell in destroying viral infected cells.[19]

Interferon production is also suppressed.[10] This ties in with the other immunologic occurrences and may be an important factor in mixed viral infections with BVD and its role in the Bovine Respiratory Disease (BRD) complex.

Since the recognition of BVD virus in 1964, the subject of vaccination has been a controversial and much debated item. The vaccine and its effects have been studied by several groups and individuals with varying, and at times, totally contradictory results. It has recently become an item of strong feeling, both pro and con, in Iowa because of its inclusion in the preconditioning program of calves sponsored by the Iowa Cattleman's Association and the Iowa AVMA.

Many practitioners strongly recommend vaccinating for BVD. Some have had no problems with vaccinating and others think the benefits obtained outweigh any problems they might encounter. Many veterinarians reason that BVD is so widespread today that a serious problem could arise if they don't vaccinate. Vaccinating the cows for BVD has proven to be a great aid for many dairymen in raising their calves and preventing the weak calf syndrome. Some veterinarians even recommend vaccinating the cow in the last trimester of gestation for maximum antibody stimulation in problem herds.[8] Several feedlot practitioners strongly recommend vaccinating cattle upon entry to prevent and decrease the severity of the BRD Complex.[4]

On the other hand, some veterinarians and owners are against vaccinating. Many of these have had or seen the results of a vaccination reaction in a herd or individual. Some are afraid of being caught in the middle of a bad situation. Some veterinarians feel that since BVD is so widespread and as there are still a lot of questions about the vaccine and BVD itself, vaccination may not be the correct way to handle it.[18]

The history and clinical signs of vaccine-related cases are generally the same. Clinical signs of an illness are usually seen ten to fourteen days following vaccination.[11] The first symptoms are anorexia, depression, and an occulonasal discharge which is serous at first and then becomes mucoid or mucopurulent. A crusting of the area around the nose and eyes may also occur. Oral ulcerations may or may not develop at this time. Next comes a severe watery diarrhea which may contain mucus and some blood. Intense straining can also occur. Some of these animals have a high fever, 104°F plus, while others maintain a normal temperature. WBC is variable but a leukopenia of all cell types is the general occurrence, especially in the early stages of the condition. Most animals become severly dehydrated. Death usually occurs in these animals in ten to fourteen days.[6] Postmortem lesions are also variable. Oral and esophageal ulcers are common as well as ulcers in the rumen, abdomen, and intestines. Lesions of Peyers' patches and changes in the spleen and lymph tissue are seen in over 50% of the cases. A moderate to severe catarrhal enteritis may be seen. Evidence of a generalized septicemia, e.g. petechiation of visceral organs, may also be found in some cases.[6]

After examining the facts, I do not believe anyone can say we do not see BVD vaccine related reactions. The cause of these reactions, however, is still a mystery. Several explanations have been proposed. One possibility is that the vaccine itself causes the condition directly. Possibly the vaccine is not modified by enough passages in the laboratory and it reverts to a somewhat virulent strain in the animal. Since BVD is so widespread and can be passed in utero, a non-cytopathic strain may be harbored in the embryonal bovine kidney cells used to grow the virus or in the embryonal calf serum used as a nutrient medium. Virus has been isolated from several calves at birth without antibody production. Maybe the working seed virus a company uses becomes contaminated by a virulent non-cytopathic virus.[5]

It has been shown in several studies that the vaccine causes a leukopenia and an immunosuppression in much the same way as the natural infection.[18] Perhaps this suppression allows an animal which is incubating a viral infection, BVD, IBR, etc., to develop the disease and show clinical signs. The sup-

pression may also allow a minor or non-pathogen to establish. Since it is known that there are inapparent carriers, this may suggest that vaccination stimulates these latent infections to become clinical cases.

Some people blame the reactions on the immuno incompetency in some animals.[1] This may be due to individual or hereditary variation. It could also be due to stress or corticosteroid treatment.[18]

As a means to decrease post vaccinal reactions, some companies have switched to growing the virus on porcine cells to make their product safer.[17] Others have switched virus strains or developed new strains of the virus.[5] Several companies are working on killed vaccine products at this time. In the past, the killed products have shown very poor antigenicity and most animals showed no serological response.[11,14]

The duration of immunity to BVD after vaccination has also been a question. At first it was thought that it gave a lifelong immunity. Today a yearly vaccination is recommended beginning at four to six months[1] (earlier if an endemic problem; as young as one month because maternal antibodies do not seem to interfere).[18]

BVD vaccine should be used with discretion. It can be of great value in many herds. It should not be given when an animal is under stress, after corticosteroid therapy, to sick animals, or with other vaccines, since it does cause an immunosuppression. I believe we will see a good killed product in the next few years and hopefully it will solve the BVD vaccination dilemma.

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